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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR RAPID IDENTIFICATION OF PATHOGENS IN HUMANS AND ANIMALS

(57) Abstract: The present invention provides methods of: identifying pathogens in biological samples from humans and animals, resolving a plurality of etiologic agents present in samples obtained from humans and animals, determining detailed genetic information about such pathogens or etiologic agents, and rapid detection and identification of bioagents from environmental, clinical or other samples.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/38761

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12P 19/34; C07H 21/02

US CL : 435/6, 91.2; 536/23.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.2; 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	MUDDIMAN et al. Characterization of PCR products from Bacilli using electrospray ionization FTICR Mass spectrometry. Analytical Chemistry. 01 November 1996, Vol. 68, pages 3705-3712, see entire document.	1-6, 27-39 --- 7, 9-24
Y	US 6,043,031 A (KOSTER et al) 28 March 2000 (28.03.2000), see entire document.	1-7, 9-24, 27-39
Y	BORROW et al. SiaD PCR Elisa for confirmation and identification of serogroup Y and W135 meningococcal infections. FEMS Microbiological Letters. 1998, Vol. 159, pages 209-214	9-24
Y	BOIVIN-JAHNS et al. Bacterial diversity in a deep subsurface clay environment. Applied and Environmental Microbiology. September 1996, Vol. 62, No. 9, pages 3405-3412, see page 3406, column 2, subheading "rDNA amplification".	1-7, 9-24, 27-39
Y	HURST et al. MALDI-TOF analysis of polymerase chain reaction products from methanotrophic bacteria. Analytical Chemistry. 01 July 1998, Vol. 70, No.13, pages 2693-2698, see entire document.	1-7, 9-24, 27-39

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97/37041 A2 (SEQUENOM, INC.) 09 October 1997 (09.10.1997), see entire document.	1-7, 9-24, 27-39

INTERNATIONAL SEARCH REPORT

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7, 9-24, 27-39, drawn to methods of screening for disease agents.

Group II, claim(s) 8, drawn to methods of screening for primer sets.

Group III, claim(s) 25-26, drawn to methods of pharmacogenetic analysis.

Group IV, claim(s) 40-49, drawn to primer pairs.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Each primer pair of Group IV represents a different species. There are 185 different primer pairs listed in claim 40.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: There is no special technical feature over the prior art which links Groups I-IV. Claim 1 is anticipated by Muddiman et al (Anal. Chem. (1996) 68:3705-3712) who teaches a method of identifying a bioagent which is unknown comprising (a) contacting nucleic acid from the bioagent with a pair of primers which hybridize to sequences that flank a variable region (see page 3707, column 1, where the primers are drawn to the 16S and 235 rRNA sequences, which are variable at some level at those locations) (b) amplifying the variable nucleic acid sequence to produce an amplification product (see page 3707, column 1), (c) determining the molecular mass of the amplification product by a biomass detection method, here FTICR Mass spectrometry (see page 3707, column 2), (d) comparing the molecular mass to molecular masses of known bioagents thereby identifying the "unknown" bioagent (see figures 2,-5 where the masses of two different species are compared).

Since claim 1 is anticipated, there is no special technical feature over the art which links the claims, rendering the lack of unity requirement proper.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The species are not structurally related and are drawn from different sequences, including the 16S rRNA, 23s rRNA and RNAse P sequences. The primers share no common core structure. Therefore, the species are not related because they share no special technical feature in common.

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

EAST, MEDLINE, BIOSIS, CAPLUS
search terms: MALDI, FTICR, mass, spectrometry, PCR, polymerase, chain, primer, oligo, DNA, nucleic, hybridize, bacteria, universal, diversity

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/38761

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-7,9-24 and 27-39

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.